

WHAT IS CLAIMED IS:

1. A composition comprising (i) intact minicells that contain a drug molecule and (ii) a pharmaceutically acceptable carrier therefor.
2. The composition of claim 1, wherein said composition contains fewer
5 than about 1 contaminating parent bacterial cell per 10^7 minicells.
3. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^8 minicells
4. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^9 minicells
- 10 5. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^{10} minicells
6. The composition of claim 1, wherein said composition contains fewer than about 1 contaminating parent bacterial cell per 10^{11} minicells.
7. A composition consisting essentially of intact minicells that contain a
15 drug molecule.
8. A targeted drug delivery method that comprises bringing bispecific ligands into contact with (a) bacterially derived minicells that contain a drug molecule and (b) target mammalian cells, such that (i) said bispecific ligands cause said minicells to bind to said mammalian cells, (ii) said minicells are engulfed by said
20 mammalian cells, and (iii) said drug is released into the cytoplasm of said mammalian cells.
9. The method of claim 8, wherein said target mammalian cells are non-phagocytic cells.
10. The method of claim 8, wherein said bispecific ligand comprises
25 polypeptide or carbohydrate or glycopeptide.

11. The method of claim 8, wherein said bispecific ligand comprises a first arm that carries specificity for a bacterially derived minicell surface structure and a second arm that carries specificity for a non-phagocytic mammalian cell surface receptor.

5 12. The method of claim 11, wherein said first arm and said second arm are monospecific.

13. The method of claim 11, wherein said first arm and said second arm are multivalent.

14. The method of claim 11, wherein said minicell surface structure is an
10 O-polysaccharide component of a lipopolysaccharide on said minicell surface.

15. The method of claim 11, wherein said minicell surface structure is a member of the group consisting of outer membrane proteins, pilli, fimbriae, flagella, and cell-surface exposed carbohydrates.

16. The method of claim 11, wherein said mammalian cell surface receptor
15 is capable of activating receptor-mediated endocytosis of said minicell.

17. The method of claim 8, wherein said bispecific ligand comprises an antibody or antibody fragment.

18. The method of claim 8, wherein said bispecific ligand comprises a humanized antibody.

20 19. The method of claim 8, wherein said minicell comprises an intact cell wall.

20. The method of claim 8, wherein said drug is a chemotherapeutic agent.

21. The method of claim 8, wherein said mammalian cells are *in vitro*.

22. The method of claim 8, wherein said mammalian cells are *in vivo*.

23. The method of claim 8, wherein said drug is encoded on a plasmid contained within said minicells.

24. The method of claim 23, wherein said plasmid comprises a regulatory element.

5 25. The method of claim 23, wherein said plasmid comprises a reporter element

26. A drug delivery method that comprises bringing bacterially derived minicells that contain a drug into contact with mammalian cells that are phagocytosis- or endocytosis-competent, such that said minicells are engulfed by said mammalian
10 cells and said drug is released into the cytoplasm of said mammalian cells.

27. The method of claim 26, wherein said minicells comprise an intact cell wall.

28. The method of claim 26, wherein said drug is a chemotherapeutic agent.

15 29. The method of claim 26, wherein said minicells are *in vitro*.

30. The method of claim 26, wherein said minicells are *in vivo*.

31. The method of claim 26, wherein said drug is encoded on a plasmid contained within said minicells.

20 32. The method of claim 31, wherein said plasmid comprises a regulatory element.

33. The method of claim 31, wherein said plasmid comprises a reporter element.

25 34. A method of loading minicells with a drug, comprising the step of creating a concentration gradient of said drug between an extracellular medium containing said minicells and the minicell cytoplasm, such that said drug moves down said concentration gradient, into the minicell cytoplasm.

35. A method of loading minicells with a drug, comprising the steps of:
(a) culturing a recombinant parent bacterial cell capable of producing minicells under conditions such that said parent bacterial cell transcribes and translates a therapeutic nucleic acid encoding said drug, such that said drug is released into the cytoplasm of said parent bacterial cell, and then
5 (b) allowing said parent bacterial cell to form one or more minicells containing said drug in their cytoplasm.

36. A method of loading minicells with a drug, comprising the step of culturing a recombinant minicell that contains a therapeutic nucleic acid encoding
10 said drug under conditions such that said therapeutic nucleic acid encoding said drug is transcribed and translated within said minicells.

37. A composition comprising (i) a bacterially derived minicell that contains a drug molecule and (ii) a bispecific ligand that is capable of binding to a surface component of said minicell and to a surface component of a non-phagocytic
15 mammalian cell.

38. Use of bacterially derived intact minicells and bispecific ligands in the preparation of a medicament, said minicells containing a drug molecule and said bispecific ligands being capable of binding to said minicells and to target non-phagocytic mammalian cells, for use in a method of treating a disease or modifying a
20 trait by administration of said medicament to a cell, tissue, or organ.